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THE CLINICAL FEATURES OF CASES OF SUBACUTE BACTERIAL ENDOCARDITIS THAT HAVE SPONTANEOUSLY BECOME BACTERIA-FREE.[1]

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At the meeting of the Association of American Physicians in 1912, the writer[2] presented a paper on the results of a study of the endocardial lesions found in cases of subacute bacterial endocarditis (chronic malignant endocarditis, chronic infectious endocarditis, chronic ulcerative endocarditis, endocarditis lenta). After describing these lesions he presented evidence that the bacteria in such cases could spontaneously disappear from the lesions and that the lesions could heal in part or entirely. It was shown that the healing of the lesions was not necessarily accompanied by recovery from the clinical standpoint. There are two reasons for this. In the first place the healing of the lesions leaves fibrous and calcareous tags or masses, which interfere with the usually already improper functioning of the valves and the musculature of the heart, and which may give rise to embolic phenomena. In the second place so much injury may be done to the kidneys and the blood-forming organs that although the bacteria disappear the damaged tissues cannot functionate to the extent necessary for the preservation of life.

In the paper referred to there were briefly presented notes on eleven cases, concerning which there was no doubt that the patients

[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May 8, 1913

[2] Libman, Amer. Jour. Med. Sci., September, 1912, cxliv, 313; Trans. Assoc. Amer. Phys., 1912, xxvii.

had suffered from subacute bacterial endocarditis and had spontaneously become bacteria-free. In three of these cases (these were the earliest cases) the condition was not suspected clinically, and the diagnosis was established by the evidence accumulated by a study of the postmortem material. In the other cases the diagnosis was made from the clinical features and proved by bacteriological and pathological investigations. The presence of the embolic glomerular lesions in the kidneys, described by Loehlein, and later by Baehr[3] and Gaskell, we found to be pathognomonic of the existence of subacute bacterial endocarditis when due to the cocci usually found in such cases. In those cases which were due to the influenza bacillus, such lesions were not found. As these cases are quite infrequent, this is not evidence that such lesions cannot be produced by subacute or chronic endocarditis due to this organism.

It is my present purpose to give a short review of the clinical features of the bacteria-free cases that we have observed up to to the present time. As it would not be possible, except in monographic form, to discuss these cases in detail, only certain important points will be mentioned. There will be appended a short description of the clinical course of each of the cases which were utilized in the course of the study.

In the earlier paper the following description was given of the clinical course of the cases seen up to that time:

1. They may develop a nephritis and die of uremia.

2. They present the picture corresponding to what we have been wont to call chronic endocarditis with fever (that is, they have a valvular lesion, more or less fever from time to time, usually low, occasional petechiæ, occasional joint symptoms, and embolisms). Some of these cases resemble cases in which bacteria are demonstrable in the blood. Some are pale, others more or less pigmented.

3. Some of the cases present a complex that appears to have been entirely overlooked. The striking feature is a peculiar diffuse brown (sometimes quite dark) color of the face. The rest of the body may show some pigmentation. There is evidence of a valvular lesion, there is more or less anemia, usually a palpable spleen, and usually also tenderness of the sternum. The patients feel weak and do not sleep well. Petechiæ occasionally occur. There is fever from time to time, usually low. Erythrocytes are found in the urine in some of the cases. The subsequent history of such cases is not yet known; one case died with symptoms of cerebral embolism. The important feature of these cases is the curious change in the color of the face. Since I have observed it in bacteria-free cases, I have looked for it in cases in the bacterial

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[3] Amer. Jour. Med. Sci., September, 1912, cxliv, 327.

stage, and, to my surprise, I find that while the faces of most of the cases are sallow, or of a rather white color, some develop a certain amount of brown or café-au-lait color.

4. They may go on with more or less anemia, and suffer from that and from decompensation.

In discussing the splenic enlargement which occurs in the bacteria-free as well as in the bacterial stage, I suggested that from observations made several years before, I had reason to believe that a case would occasionally be found in the bacteria-free stage in which marked enlargement of the spleen might be a very conspicuous feature of the case. I suggested that when such a case did come under observation, it might be regarded as a case of Banti's disease plus chronic valvular disease, and that it might not be recognized that the case was really one of subacute bacterial endocarditis in the bacteria-free stage, with marked enlargement of the spleen as the most conspicuous feature. During the last year I saw a case which showed that such a clinical picture is possible. A description of it is appended (Case XXI).

I have given the classification which I described in the paper published last year, because it is the basis of my present classification. After describing the mode of onset, the symptoms, and the termination of the cases in the bacteria-free stage, I shall show in what way I have found it necessary to modify the classification.

The remarks which follow are based on a study of 21 cases of subacute bacterial endocarditis in the bacteria-free stage; 4 of the cases are still alive. Postmortem examinations were made in 17 of the 18 cases that succumbed, and in all there was ample proof from the clinical, bacteriological and pathological studies that we were dealing with the disease under discussion. In the course of the investigations, 1 case was encountered which was suspected of being in the group, but there was not sufficient evidence present at the postmortem examination to corroborate the clinical suspicion. This case is mentioned among the appended notes, but is not described in detail. It will be of service on another occasion when the question of differential diagnosis is taken up. Up to May, 1910, the writer had observed 43 cases of subacute bacterial endocarditis.[4] Since that time he has made more or less comprehensive studies of 82 more cases, the entire number being 125. Of the 82 cases seen since May, 1910, 18, or over one-fifth, were in the bacteria-free stage (1 case became bacteria-free under observation, Case VIII). The writer is convinced that a careful study of all the cases of chronic valvular disease seen at the hospital during that period would have resulted in unearthing a larger number of cases. It is only by a careful scrutiny of all cases supposed to be instances of uncomplicated chronic valvular disease that one becomes im-

[4] Cf. Libman, Amer. Jour. Med. Sci., October, 1910.

pressed with the frequency with which patients are found suffering from chronic valvular disease plus the bacteria-free stage of subacute bacterial endocarditis.

We will now proceed to a review of some of the clinical features of the disease:

DURATION. This is difficult to estimate, as most of the cases were not seen in the bacterial stage, and therefore one can have no idea of the length of the bacteria-free periods. In Case VIII, in which influenza bacilli were found for almost two months, the later bacteria-free period was about four months. There is sufficient evidence to show that the bacteria-free period may last for two and a half years, as in Case XIII. In two cases there was a history of the presence of cutaneous tender nodules three (Case XX) and three and a half years (Case XIII) before death. It is to be remembered that there are a few records in the literature of cases in which patients became bacteria-free under observation and remained well except for the presence of the previously existing valvular lesion. But the period of observation in these cases was not very long when the cases were reported, and no later reports have been issued which state whether the patients developed any of the special features to which we have drawn attention as occurring in the bacteria-free stage.

PREVIOUS HISTORY. In one case there was a history of scarlet fever at an early age. In a number of cases there was a history of previous attacks of rheumatism and of the establishment of a valvular lesion. In some cases the patients had suffered for a longer or shorter time from palpitation, dyspnea, pain in the precordial region, and cough with or without expectoration; at times the sputum was hemorrhagic.

In a few of the cases there was a history of an attack of fever, pains in the joints, palpitation, and dyspnea a number of months before the development of the symptoms for which the patient came under observation. It is proper to suspect that these attacks in some instances represent the bacterial stage of the disease. A critical analysis of the data bearing on this point will be submitted at another time.

MODE OF ONSET. In most of the cases the early symptoms were cardiac in nature. There was dyspnea, palpitation, and cough with or without hemorrhagic expectoration. With these symptoms there might or might not be chilly sensations, fever, sweats, joint pains, and swelling of the legs. In one case severe pain in the thigh was the first symptom (due to an embolic aneurysm of the femoral artery). In another a severe pain in the sacral region was the prominent early symptoms (this is at times observed also in the bacterial stage of the disease). Vomiting associated with headache and dizziness was the initial symptom-complex in a couple of cases; in one case epistaxis, and in another purpura first appeared. Frequency of urination was a striking symptom that appeared early in two cases.

FEVER. The temperature in the bacteria-free cases does not run as high as in the bacterial cases. It may be high in cases that are seen, apparently, shortly after the bacterial stage has ended, or if complications develop or an intercurrent disease. Embolisms may cause marked rises of temperature, and at times chills, even though there be no bacteria in the pieces thrown off from the valves. In many cases the temperature is practically normal during almost the entire period of observation.

VALVULAR LESIONS. In every one of the cases there was evidence of an organic lesion of the mitral or aortic valve, often of both. As a rule no new murmurs developed during the disease.

RENAL PHENOMENA. This subject is so important in connection with the symptomatology of the bacteria-free stage of subacute bacterial endocarditis that it is possible to give only the shortest account of our observations. Macroscopically, hemorrhagic urine usually occurs either when the case comes under observation shortly after the bacterial stage is ended (as made apparent by the clinical pictures or by the study of the age of the vegetations found in the heart) or as the result of gross embolic lesions of the kidney. Erythrocytes in small numbers are found in the urine in a number of the cases, but not with the regularity or persistence with which they are found in the bacterial stage of the disease.

Albumin and casts are found in some of the cases from time to time. In others there is definite evidence of a more or less marked progressive disease of the kidney. In this latter group of cases there are two types. In the one there is passed a subnormal, normal, or increased quantity of urine of a normal or subnormal specific gravity, albumin and formed elements being more or less conspicuously present. In the cases of the second type there is passed a large amount of urine (up to 2700 c.c.), with a high specific gravity (up to 1028 or 1032), and this may occur even when there are present but a few formed elements and only a trace of albumin. This second clinical type of renal disturbance has not, as far as the writer knows, been previously described. The relationship of the clinical phenomena and the pathological lesions is worthy of a special study.

Symptoms due to renal insufficiency were prominent in a number of cases; in some they dominated the clinical picture. In one case (Case III) the examination of the fundus revealed edema of the optic disks and retina. As will be seen later, renal insufficiency was the main cause of death in a comparatively large number of cases.

BLOOD CHANGES. In the cases in which examinations were made (and they were made in nearly all) there was found a more or less marked anemia, always of the secondary type. The hemoglobin in some cases was as high as 65 per cent., and in others as low as 35 or even 20 per cent. There was a tendency to progressiveness in the anemia in many of the cases. Nucleated erythrocytes were never found. The bone-marrow of the femur was examined in two cases, and was found to be dark red in color, and to show typical regenerative changes. In a third case the tibia was examined and fatty marrow found.

When the anemia was profound it was plainly revealed by the color of the skin and mucous membranes, and by a general edema most marked in the lower limbs.

The leukocytes were usually not increased in number except when complications ensued. In some cases the number diminished during the course of the disease (to 4000 at times). The polymorphonuclear cells were either normal or moderately increased (barring periods during which there were complications). In a few cases they diminished during the progress of the disease (in one case to 36 per cent.).

SPLENIC ENLARGEMENT. The spleen was palpable in all the cases except four. At times it was enormously enlarged. In all the cases but one of those in which the spleen was not palpable it was found enlarged at the postmortem examination, at times very much so. In a large percentage of the cases the Malpighian bodies in the spleen were conspicuously enlarged and, microscopically, hyperplastic.

PETECHIÆ. These were found at one time or other in 13 cases. They were located in the mucous membranes (especially the conjunctivæ) and the skin. As a rule few were found as compared with the number seen in cases in the bacterial stage.

PURPURA. This was noted in three cases. In one it was the main symptom for two months before the patient came under observation. In another case it occurred repeatedly throughout the course of the disease.

TENDER CUTANEOUS NODULES. These were found in only three cases. In two they persisted close up to the time of the fatal termination. One of these two patients had had these lesions for three years, and one for three and a half years.

STERNAL TENDERNESS. This symptom, as the writer stated last year,[5] seems to be more marked in the bacteria-free stage than in the bacterial stage. It was found in all of the cases in which it was looked for. In one case the tenderness of the lower sternum was so marked that it was elicited by the lightest tap. The long bones were usually not found tender.

SWEATS AND LOSS OF WEIGHT. These symptoms were not nearly as marked as in cases in the bacterial stage. In only a few cases is there a note of profuse perspiration. That loss of weight should not be a prominent symptom is evident from the fact that many of the cases have comparatively little fever as compared with cases in the bacterial stage.

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[5] Trans. Assoc. Amer. Phys., 1912.

PIGMENTATION. The brown color of the face was noted as a striking symptom in nine cases. In some of these it increased under observation. A few of the anemic patients whose faces were at first white, later developed a more or less marked café-au-lait tint. This has also been observed by the writer, as stated in a previous publication, in the bacterial stage, but the development of a marked brown color he has seen only in cases in the bacteria-free period.

PAINS. The only pains that occurred with any frequency were joint pains. These occurred particularly in the cases in which purpura was a symptom. Reference has already been made to the case in which pain in the sacrum was a marked feature. Pains due to various complications need no discussion here.

ANEURYSMS. Apart from the occurrence of aneurysms of the mitral valve, the septum membranaceum, and the sinuses of Valsalva, which produced no recognizable symptoms, there was encountered once an embolic aneurysm of the femoral artery. The aneurysm had ruptured into the soft parts and had eroded the bone. The patient was sent into the surgical service of the hospital with a diagnosis of osteomyelitis, because of the rapidly developing large tender swelling, the fairly high temperature, and the high leukocyte count with polynucleosis. Because of the presence of a valvular lesion, a large spleen, and a marked anemia, I suspected that we were dealing with a case of subacute bacterial endocarditis. Further observation proved that this view was correct. The postmortem examination corroborated the clinical opinion; the lesions were practically bacteria-free, and for the main part organized. This was in keeping with the fact that the three blood cultures made in the case gave a negative result.

CARDIAC SYMPTOMS. These can be classed in two groups. We must consider first the subjective and objective symptoms due to the valvular lesion as such. Here we include the palpitation, pains in the chest, dyspnea, cough and expectoration, congestion of the viscera, edema of the legs, and hemorrhagic infarction of the lungs.[6] All these symptoms may occur in any case of valvular disease.

In the second group we include the embolisms, petechiæ, purpura,[7] embolic aneurysms, and tender cutaneous nodules; this second group of symptoms occurs when there are friable masses on the valves of the heart or on the wall. They are therefore common events in cases of subacute bacterial endocarditis in the bacterial or bacteria-free stage, and may well be called endocarditic symptoms. Cerebral embolism seems to be as frequent an occurrence in bacteria-free as in bacterial cases.

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[6] These are due oftener than is generally supposed to thromboses in veins of the lower extremities or of the pelvis.

[7] This could, of course, at times be due to a hemorrhagic diathesis.

JOINT SYMPTOMS. These are much less common than they are in the bacterial stage. There may be joint pains or joint swellings, or both. Occasionally, as stated above, purpura is also present. The joint swellings are, as a rule, not marked, and are quite transitory. The writer does not remember having seen a joint that was tender or over which the skin was red.

CAUSE OF DEATH. The cause of death can be fairly definitely stated in 16 of the fatal cases: In 3 it was due to cerebral embolism, in 4 to uremia, in 2 to the progressive anemia and an intercurrent pneumonia, in 1 to uremia, embolism, and pneumonia, in 1 to pneumonia, in 3 to cardiac insufficiency, in 2 to progressive anemia, with concomitant cardiac weakness. To put the matter in another way, it may be said that cerebral embolism was a determining factor in 4 cases, uremia in 5 cases, intercurrent pneumonia in 4 cases, anemia in 4 cases, and cardiac insufficiency (unaccompanied by profund anemia) in 3 cases.

The important role played by the progressive anemia, the nephritic changes, the presence of vegetations on the valves, and the improper functioning of the valves and musculature of the heart is thus made very clear.

The lesions found in the heart in all the cases were, in the main, of the same type as those described in the writer's earlier paper on this subject. In two cases atypical lesions were found, the main feature of which was a peculiar worm-eaten appearance of the mitral valve, which in both instances was the seat of an old mitral stenosis (Cases XIII and XX). In one of these two cases the glomerular lesions were of a diffuse type and the typical embolic lesions were not present. The clinical history was, however, quite typical, and the characteristic tender cutaneous nodules were seen by the writer.

GENERAL GROUPING OF THE CASES. From the description which we have just given of the symptomatology of the disease under consideration it might appear that most of the cases look quite alike clinically. But while it is true that petechiæ, sternal tenderness, a palpable spleen, and a more or less marked anemia occur in most instances, the cases can be grouped according to certain features that particularly impress the observer. In the earlier part of this paper the writer quoted the classification of the cases that he attempted to make and which he presented last year, and he also drew attention to the occasional occurrence of an unusual enlargement of the spleen. The study of the additional cases seen since then, in conjunction with a review of the earlier cases, leads him to describe five prominent features, one or more of which may be found in a certain case, and characterize the case rather than describing four or five groups; for he has found there are cases that belong to more than one of the groups which he described last year.

The five prominent features which may be found are:

1. Marked progressive anemia.
2. Brown pigmentation of the face.
3. Marked evidence of renal disease.
4. Marked enlargement of the spleen. The spleen may be so enlarged that the case may be considered a case of chronic valvular disease associated with Banti's disease.
5. Phenomena due to the vegetations present on the valve. These are what I term endocarditic symptoms. They consist of more or less elevation of temperature occurring from time to time, petechiæ, occasional joint symptoms, and embolisms.

Whenever any of these clinical features are found in a case of chronic valvular disease it is of the greatest importance, for it draws attention to the possibility that the case is one of chronic valvular disease plus subacute bacterial endocarditis in the bacterial or bacteria-free stage.

Afebrile or nearly afebrile periods of fair duration (several weeks) or negative results of blood-cultures would help make the differentiation between the two stages.[8] The diagnosis from certain cases of acute rheumatic infection of a valve previously the site of disease, and from some other conditions may present difficulties. The writer will not discuss this question, as it is his purpose at the present time to describe clinical features and not differential diagnosis. All he wishes to state now is that studies made by Dr. D. J. Kaliski and Dr. P. Aschner have not demonstrated the value of complement fixation tests as an aid in the diagnosis of bacteria-free cases.

In the appended description of our cases, summaries are given which show which of the five important features of the bacteria-free cases occurred in each. A few examples will, however, be of interest here:

Case I. Pigmentation; endocarditic symptoms.

Case III. Nephritic symptoms.

Case V. Endocarditic symptoms; progressive anemia.

Case VI. Endocarditic symptoms; intense anemia; pigmentation.

Case XV. Pigmentation.

Case XXI. Marked splenic enlargement; progressive anemia; renal symptoms.

Description of Clinical Course of Cases. In the following notes there will be presented a concise description of all the cases of subacute bacterial endocarditis in the bacteria-free stage that the writer has observed. As the cardiac lesions were described rather fully in the paper presented before the Association last year, and as it is his purpose at another time to publish an account of these lesions in greater detail, he will, in the descriptions of the cases, refer to the postmortem findings in as brief a manner as possible. The renal lesions will also not be described at the present time, as they will form the basis of another communication. It is sufficient to state that in nearly all the cases the embolic glomerular lesions, which are characteristic of the disease (except when due to the influenza bacillus), were present. In a few cases these embolic lesions were associated with other diffuse glomerular lesions. In a few cases only diffuse lesions of the glomeruli were present. These lesions will be described at another time. In the few cases in which embolic lesions were not present, there was sufficient evidence present clinically (tender cutaneous nodules) or at the postmortem examination to put the cases into the group which the writer has termed subacute bacterial endocarditis in the bacteria-free stage.

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[8] It is an interesting fact that in cases of subacute bacterial endocarditis in the bacterial stage, bacteria can practically always be found in the blood if the temperatures are not elevated a great deal. It is in the cases with high temperatures and with very marked oscillations that one fails at times to obtain bacteria in the blood cultures although the bacteria are present in enormous numbers in the vegetations in the heart.

A perusal of the following notes will show that the writer has included four patients who are still alive, all of whom are in quite good condition. Although the absolute evidence of the fact that they belong in this group is not forthcoming, the cases are so typical clinically and correspond so closely to other cases in which the clinical diagnosis was proved correct by postmortem examination that it seemed desirable to include them.

Case I.—Observed from July 2, 1905, to August 6, 1905. Three blood-cultures were made, with negative results. There was a previous history of scarlet fever at the age of two years; pains and redness of the joints during the last winter. Onset one month before admission, with cough and expectoration, cardiac palpitation, dyspnea, pain in both knees, which were red and not swollen. The heart showed evidences of an aortic lesion. The face was markedly pigmented. The spleen was palpable and petechiæ were present. An embolic aneurysm of the iliac artery developed. The patient passed large amounts of urine, up to 2000 c.c. a day, containing a moderate number of leukocytes and hyaline casts. The leukocyte count varied from 6200 to 9200; hemoglobin, 65 per cent., later 61 per cent. The temperature rose at the highest to 101° or 102°, except just before the embolism occurred, due to which the aneurysm developed; at that time the temperature was 104°. The cause of death was apparently a cerebral embolism. Postmortem examination revealed a healed clacareous bacteria-free lesion[3] of the aortic valve, with an aneurysm of the mitral valve and fibrous lesions of the chordæ tendineæ. The spleen was large and showed marked hyperplasia of the Malpighian corpuscles and one infarction. In the kidney there was an embolic aneurysm.

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[3] This means that the cultures from the centre of the vegetations showed no bacteria, and that smears made from crushed vegetations also showed no organisms.

SUMMARY. The main features in this case were pigmentation and endocarditic phenomena (development of non-bacterial embolic aneurysms).

CASE II.—Observed from May 1, 1907, to October 3, 1907. There were two blood-cultures, with negative results. There had been cardiac palpitation and dyspnea for six months. For two months prior to admission, attacks of purpura, and for five weeks edema of the legs, were present. The cardiac lesion was apparently aortic insufficiency. The spleen was palpable just below the free border of the ribs and petechiæ were present. Perspiration was a marked feature. The urine varied in amount from 750 to 850 c.c. Specific gravity ranged from 1008 to 1012; erythrocytes were present, also hyaline and hyalogranular casts. Blood examination at first showed 5200 leukocytes, 53 per cent. hemoglobin, and 3,040,000 erythrocytes. Later the leukocyte counts varied from 4000 to 7000; the polymorphonuclear count was as low as 41 per cent., except a short time before death, when it was 68 per cent. The hemoglobin dropped to 38 per cent. The temperature was usually around 100°, occasionally 101°, except when an embolism occurred or when a purpuric rash developed. Death was due to cerebral embolism. The autopsy showed a calcareous lesion of the aortic valve and an aneurysm of the membranous septum. The spleen was almost twice the normal size, contained old and recent infarctions, and the Malpighian bodies were prominent. Areas of softening were found in the brain.

Summary. The important features of this case were endocarditic phenomena (embolisms and purpura), the marked enlargement of the spleen, the urinary phenomena, progressive anemia, and lymphocytosis.

CASE III.—Observed from November 9, 1905, to May, 1906, and again from October 3, 1909, to November 3, 1909. There was one blood-culture, with negative result. A history was obtained of rheumatism occurring two years before the date of the first admission. During the first stay in the hospital there were joint symptoms and a pericarditis. Hemoglobin was 86 to 90 per cent., but progressively dropped to 65 per cent. The temperature was at first up to 103°, afterward practically around normal, except with occasional rises to 101° or 101.2°. The quantities of urine varied from 620 to 1600 c.c. The specific gravity varied between 1008 and 1028, being usually around 1010 to 1020; there was present a faint trace of albumin, and occasional hyaline and hyalogranular casts. The spleen was not palpable. There were evidences of mitral insufficiency. On admission the second time the patient gave a history of having developed edema of the legs five weeks before. Ophthalmoscopical examination showed marked edema of the optic disks and surrounding retina. Hemoglobin dropped to 36 per cent. Urine quantity varied at first from 1300 up to 3000 c.c., and later dropped to 330 c.c. At the time of the second admission the urine contained a trace of albumin, numerous hyaline and granular casts, and leukocytes; later it was reddish brown in color, contained a heavy trace of albumin and numerous erythrocytes. The patient died of uremia. At autopsy there was found a fibrous lesion of the wall of the left auricle and fibrous and calcareous lesions of the chordæ tendineæ. The spleen was one and a half times the normal size.

Summary. The main features of this case were the progressive anemia and the renal phenomena.

CASE IV.—Observed from April 24, 1910, to May 9, 1910. There was one blood culture, with negative result. The patient had been dyspneic for one year. For two weeks there was vomiting, headache, and dizziness. There was evidence of mitral and aortic insufficiency; the spleen was palpable. There were no petechiæ. The patient looked anemic. Hemoglobin was 60 per cent.; leukocytes, 13,000; polymorphonuclears, 65 per cent. The urine varied in specific gravity from 1010 to 1013; there was present a faint trace of albumin; occasional hyaline casts, erythrocytes, and granular casts. The temperature was never over 102°, usually between 99° and 100°. The patient died of uremia, cerebral embolism, and a terminal pneumonia. The autopsy showed old pericardial adhesions and a lesion of the wall of the left auricle and of the chordæ tendineæ, which was almost entirely healed. The spleen was one and a half times the normal size, and contained infarctions.

Summary. Renal phenomena, old pericarditis, moderate anemia.

CASE V.—Observed from July 14, to October 8, 1910. There were three blood cultures, with negative results. There was a history of articular rheumatism at the age of six years, and of palpitation and dyspnea since that time. The onset of the present illness occurred ten weeks before admission to the hospital, with pain in the thigh, swelling, and limping, all this being due to a ruptured embolic aneurysm of the femoral artery. The heart showed evidences of mitral and aortic insufficiency. The spleen was large (the spleen was particularly large in view of the fact that the boy was sixteen years of age and much undersized). There was a café-au-lait color to the face. The urine at first showed a specific gravity of 1020, later 1004 up to 1020; there were present erythrocytes and hyalogranular and granular casts. The blood count showed 15,200 leukocytes; 65 per cent. polymorphonuclears and a hemoglobin content of 20 per cent.; later the leukocyte count was 8400; polymorphonuclears 36 per cent., and the hemoglobin dropped to 17 per cent. The temperature was usually up to 102°. Death occurred from progressive anemia and a terminal pneumonia. The autopsy showed lesions of the mitral valve, chordæ tendineæ, and auricular wall, most of which were healed. In one part of the lesion there were found a few poorly staining cocci. The spleen weighed 510 grams (17 ounces); Malpighian bodies large.

Summary. Embolic aneurysm; marked splenic enlargement; renal phenomena; progressive anemia.

Case VI.—Case observed from June 26, 1911, to April, 1912. There were nine blood-cultures, with negative results. There was a previous history of rheumatism. The onset occurred three months before admission, with increase of a previously existing palpitation and dyspnea. There was frequent urination. The heart gave evidence of an aortic lesion. There was marked pigmentation of the face. The spleen was palpable. Numerous petechiæ occurred often. There were hemorrhages from the gums. There were tender nodes on the hands and feet on August 30 and October 4, and even as late as March 1. The lower sternum became distinctly tender under observation. The urine was at first grossly bloody, later erythrocytes were found microscopically from time to time. The specific gravity varied from 1020 to 1022; the amounts of urine were from 1100 to 2400 c.c. The blood-examination showed a hemoglobin content of 39 per cent. at first; this then dropped somewhat lower, and a transfusion was done and the hemoglobin brought up to 55 per cent. It then rose to 61 per cent., but later dropped again. Leukocyte count was 10,400; polymorphonuclears, 81 per cent. The temperature was at first 101° to 102°, and later was occasionally as high as 101°, except just before crops of petechiæ developed. Death was due to progressive anemia and a terminal pneumonia. At the postmortem examination there were found calcareous and fibrous lesions of the aortic valve and aneurysms of the sinuses of Valsalva. The spleen was one and a half times the normal size; there was marked enlargement of the Malpighian bodies. The bone-marrow of the femur was red, and microscopically there were evidences of regeneration.

Summary. Pigmentation; renal phenomena; progressive anemia; tender nodes present long after the active stage of the disease was passed; hemorrhagic tendency; endocarditic symptoms.

Case VII.—Period of observation from April 16, 1911, to June 13, 1911. Cultures of the blood were not made during life, but at the postmortem examination the blood was found free from bacteria, as were also the cardiac lesions. There was a previous history of acute articular rheumatism and of cardiac disease. The patient suffered from dyspnea, pain over the heart, cough, and hemoptysis. The present illness began two weeks before the date of admission, with dyspnea, orthopnea, pains about the heart, cough, and expectoration, which was a times hemorrhagic. Examination showed insufficiency of both aortic and mitral valves. Spleen not palpable. No petechiæ. Urine showed a specific gravity of 1020 to 1026, and contained a trace of albumin. The quantities varied from 1400 to 1900 c.c. The temperature was usually up to 101° or 101.2°, later at one time up to 102°. The patient developed uremia and died suddenly, the explanation of the sudden death being unknown (the writer did not observe this case himself). At the postmortem examination there was found an adherent pericardium and a bacteria-free and partially healed lesion of the chordæ tendineæ, mitral valve, and auricular wall. The spleen weighed 570 grams (19 ounces), and contained infarctions.

Summary. Renal phenómena; marked splenic enlargement.

Case VIII.—Period of observation from July 17, 1911, to October 14, 1911. In this case the first five blood-cultures gave growths of the influenza bacillus, three later ones remained sterile, the first of the latter being taken on September 9. The patient was told two years before the onset of the present illness that he had endocarditis. For eighteen months he had had pain in the ankles and feet, and had lost weight. On admission he complained of throbbing in the head, fever, and weakness. There were evidences of aortic insufficiency and mitral stenosis. At first the spleen was felt two fingers below the free border, and later four fingers below the free border. Petechiæ were present. The specific gravity of the urine varied from 1008 to 1024, later from 1011 to 1020; erythrocytes and hyaline and granular casts were present. Blood-count showed leukocytes, 6800; polymorphonuclears, 75 per cent.; hemoglobin, 64 per cent.; later the hemoglobin was 71 per cent, leukocytes 5800, and polymorphonuclears 42 per cent. The patient left the hospital some time after the blood was bacteria-free, and developed a marked progressive anemia and hydremia. At first the temperature was 104°, later not above 102°. The patient died of progressive anemia and exhaustion. An autopsy was not permitted.

Summary. Influenza bacillus infection; the case later became bacteria-free; progressive anemia; marked enlargement of the spleen.

Case IX.—Period of observation from August 8, 1911, to August 24, 1911. Two blood-cultures were taken, with negative results. The patient had previously been in the hospital from September 24, 1910, to October 15, 1910. On the first admission there was a history that the patient had had rheumatism since he was fifteen years old. Six months before the day of the first admission the patient was taken sick with fever and pain in various joints. He had marked sweats, occasional dyspnea, palpitation, and pain over the heart. The face was of a brownish color. Examination of the heart revealed mitral insufficiency and aortic insufficiency. The spleen was palpable one and a half fingers below the free border. Petechiæ and purpura both occurred. The lower sternum was distinctly tender. Urine showed a specific gravity of 1018 to 1020, a faint trace of albumin, some hyaline casts, and a few leukocytes. Blood examination at first showed leukocytes, 11,000; polymorphonuclears, 74 per cent.; later blood count showed leukocytes, 6000; polymorphonuclears, 74 per cent. On the day of admission the temperature was 103°, but after that did not rise above 100°. The patient died of cardiac insufficiency and uremia. Postmortem examination showed a bacteria-free calcified and ulcerative lesion of the aortic valve. The spleen weighed 210 grams (7 ounces); old infarctions were present; Malpighian bodies were prominent.

Summary. Pigmentation; endocarditic symptoms.

CASE X.—Period of observation from November 27, 1911, to January 31, 1912. Three blood-cultures remained sterile. Patient was taken sick, three weeks before admission, with dyspnea, cardiac palpitation, and nocturnal frequency of urination. There was marked brown pigmentation of the face. Examination of the heart revealed insufficiency of the aortic and mitral valves. The spleen was not palpable until shortly before death, when it was felt two fingers below the free border of the ribs. Petechiæ were present. The sternum was tender. Urine examination showed a specific gravity of 1016 to 1028, a trace of albumin, and occasional erythrocytes. Quantities of urine varied from 1500 to 2300 c.c. Blood-examination showed leukocytes, 9200; polymorphonuclears, 61 per cent.; later examination showed leukocytes, 7500; polymorphonuclears, 59 per cent.; hemoglobin, 65 per cent. The temperature was often up to 101° at first, and later 100° (except for rises due to an infection of the maxillary antrum and due to an acute otitis media). Death appeared to be due to embolism. Postmortem examination showed bacteria-free lesions of the aortic and mitral valves. The spleen weighed 420 grams (14 ounces), contained infarctions, and the Malpighian bodies were prominent.

Summary. Pigmentation; renal phenomena; embolism. This is one of the cases in which the patient passed large amounts of urine of high specific gravity.

CASE XI.—Period of observation from December 26, 1911, to January 30, 1912. The patient had previously been in the hospital from March 18 to April 15, 1911. Three blood-cultures were taken, with negative results. On the first admission there was cough and palpitation. Petechiæ were present. Temperature 101°, later 100°. Two days before the date of the second admission there was pain in the right forearm, due to embolism of the brachial artery just before its bifurcation. Examination of the heart revealed insufficiency of the aortic and mitral valves. Spleen was not palpable. Petechiæ were present. The sternum was tender. The urine varied in amount from 900 to 1300 c.c., contained albumin and casts, but no erythrocytes. Blood examination showed leukocytes, 11,000; polymorphonuclears, 71 per cent. There is no record of a hemoglobin estimation, but the patient looked anemic. The temperature was at first 102°, later 101°. Death was due to cardiac insufficiency and anemia. At the postmortem examination there was found a bacteria-free healed lesion of the mitral valve and the chordæ tendineæ. The spleen weighed 135 grams (4½ ounces); there were infarctions present; Malpighian bodies were prominent.

Summary. Endocarditic phenomena and anemia.

Case XII.—Period of observation from December 28, 1911, to December 31, 1911. One blood-culture was taken, with negative result. The patient had previously been in the hospital from March 24, 1905, to April 11, 1905, and from April 20, 1909, to May 1, 1909. There was a previous history of acute rheumatism. During the first two admissions he was supposed to be suffering from chronic endocarditis and rheumatism. At the time of the last admission he had been sick for four weeks, complaining of dyspnea, cough, cardiac palpitation, night sweats, and chilly sensations; he was very pale. There was marked sternal tenderness. The temperature never rose over 101°. The quantity of urine was at first 2700 c.c., and later dropped to 800 c.c. The urine showed a specific gravity of 1025 to 1028, later 1011. Blood-examination showed leukocytes, 10,000; polymorphonuclears, 78 per cent.; hemoglobin, 53 per cent. The patient died of cardiac insufficiency (and secondary renal insufficiency). Postmortem examination showed slight lesions of the aortic valve and marked lesions of the mitral valve, both bacteria-free. The spleen weighed 540 grams (18 ounces); there were infarctions present.

Summary. Moderately marked anemia; renal phenomena; marked splenic enlargement.

Case XIII.—Period of observation from January 10, 1912, to March 21, 1913. The patient had been at the hospital from January 10, 1912, to March 5, 1912. There were four blood cultures, with negative results. On the first admission to the hospital the patient was suffering from chronic endocarditis, with pulmonary infarctions and a cerebral hemorrhage (as proved by the bloody character of the lumbar puncture fluid, which was obtained at the time). When admitted on January 10, 1912, he gave a history of having had rheumatism eight years before, and since that time frequent attacks of pain about the heart and shortness of breath and also pains in the extremities. Two weeks before admission he was taken sick with a severe pulmonary hemorrhage; he was also suffering from pains in the region of the heart and the left shoulder-joint, and marked weakness. He developed a brown color of the face under observation. There was sternal tenderness present. The cardiac examination revealed a mitral insufficiency and stenosis and aortic insufficiency. He had repeated attacks of purpura. Tender nodes occurred in November, 1912, and the patient stated that he had had them already three years before. The urine varied in amount from 1700 to 2000 c.c.; the specific gravity was as high as 1030; there were hyaline casts present. During the period of observation there were several attacks of hematuria. Toward the latter part of the disease no erythrocytes were found. There were two attacks of cerebral embolism. The temperature was usually around 99°, except when embolic phenomena or pulmonary infarctions developed. The patient died of cardiac insufficiency. Postmortem examination showed old, bacteria-free, fibrous lesions of the aortic valve and ulcerative and fibrous lesions of the mitral valve, also bacteria-free. The spleen weighed 240 grams (8 ounces) and was scarred from infarctions. The bone-marrow of the tibia was fatty (that of the femur could not be obtained).

Summary. Endocarditic symptoms (embolisms, purpura); pigmentation; renal phenomena; anemia. Special note is to be made in this case of the excretion of large quantities of urine of high specific gravity (the urine contained few or no formed elements when a large amount of concentrated urine was being passed).

CASE XIV.—Period of observation from February 1, 1913, until the present time, the patient being alive and in little worse condition than when first seen. There were five blood-cultures made, all with negative results. The main features of this case were pigmentation of the face and exqisite tenderness of the lower sternum. The spleen was palpable at one time, and petechiæ were present in the conjunctivæ during the early part of the observation. The patient is in the hospital at the present time suffering from mitral insufficiency, with attacks of decompensation and acute bronchitis.

CASE XV.—Period of observation from September 4, 1911, until the present time, the patient still being alive. One blood-culture was taken, with negative result. This patient suffering from insufficiency of the aortic and mitral valves. He showed marked pigmentation of the face and marked sternal tenderness. The spleen was palpable. He passed large quantities of urine, as high as 2350 c.c. The specific gravity of the urine varied from 1018 to 1027; there was a faint trace of albumin, and erythrocytes were found from time to time. The blood-examination showed leukocytes, 8800; polymorphonuclears, 48 per cent.

CASE XVI.—Period of observation from June 4, 1912, until the present time, the patient being still alive. Two blood cultures were made, with negative results. The patient gave a previous history of rheumatism. Two days before admission to the hospital he was taken sick with dyspnea and cardiac palpitation and pain. Face was markedly pigmented, and there was marked sternal tenderness. Petechiæ were found, and there were evidences of mitral insufficiency. He was becoming progressively more pale, and had lost weight. He was passing from 2800 to 2900 c.c. of urine; specific gravity, 1008 to 1020; some albumin, hyaline and granular casts, and erythrocytes. Blood count showed leukocytes, 10,000; polymorphonuclears, 65 per cent.; hemoglobin, 50 per cent. The temperature ran from 101° to 102°, and once was 103°.

These last three cases appear to the writer to belong with great certainty, to the group under discussion. Cases XV and XVI are both working at the present time; Case XIV is up and about and is staying in the hospital because of the repeated attacks of bronchitis and asthma. These cases are identical with others that were picked out as clinically belonging in the group, and in which the diagnosis was confirmed by postmortem examination.

Case XVII.—Period of observation from August 22, 1912. to August 30, 1912. There was one blood-culture, with negative result. There was a previous history of rheumatism. Five weeks before admission to the hospital the patient complained of headache, fever, and chilly sensations. Examinations of the heart revealed insufficiency of the aortic and mitral valves. The patient appeared anemic. Petechiæ were present, and also marked tenderness of the sternum. Urine examination was practically negative. Blood-examination showed leukocytes, 12,000; polymorphonuclears, 76 per cent. The spleen was palpable two fingers below the free border. The temperature never rose above 100.6°. Death was apparently due to embolisms. Postmortem examination showed bacteria-free old lesions of the aortic and mitral valves. The spleen weighed 540 grams (18 ounces); there was marked hyperplasia of the Malpighian bodies; old infarctions were also present. The bone-marrow of the tibia was found to be red in color and microscopically showed changes found in bone-marrow regeneration.

Summary. Embolic phenomena; marked splenic enlargement; regeneration of the bone-marrow in the femur.

Case XVIII.—This case will not be discussed in detail at the present time. It is the case mentioned above which was suspected of belonging in the group in which there was not sufficient evidence at the postmortem examination to corroborate the clinical diagnosis. It will be described in detail at another time.

Case XIX.—Period of observation from September 16 to the present time, the patient being still alive. One blood-culture was taken, with negative result. This case is only suspicious and cannot be considered to surely be a case in the group. Three years before admission the patient was suffering from dyspnea and palpitation. There was marked brown pigmentation of the face. There was present a stenosis and insufficiency of the mitral valve and insufficiency of the aortic valve. Spleen was palpable. The sternum was distinctly tender. Quantities of urine varied from 700 to 950 c.c.; specific gravity ranged from 1010 to 1026; there was a faint trace of albumin, some leukocytes, and a few erythrocytes. Blood-count showed leukocytes, 7200; polymorphonuclears, 63 per cent.;

erythrocytes, 5,792,000; hemoglobin, 60 per cent. The temperature was practically normal.

CASE XX.—Period of observation from September 17, 1912, to October 19, 1912. One blood-culture was made, with negative result. The patient was taken sick, one week before admission, with dyspnea, pain the chest, cough, with bloody expectoration, and swelling of the feet. He stated that he had had lesions that corresponded to the tender cutaneous nodules of subacute bacterial endocarditis on three fingers of the left hand three years before admission. The heart presented evidences of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable. The patient looked anemic. The sternum was markedly tender. On September 13 the patient developed tender nodules on the thumb of the left hand, and he had had one on the right hand two weeks before. The quantity of urine passed was as high as 2400 c.c. a day; specific gravity varied from 1012 to 1016; erythrocytes were present, also granular and waxy casts. Blood-count showed leukocytes, 13,400; polymorphonuclears, 58 per cent. There was no record of any hemoglobin estimation, but the patient was evidently anemic. The temperature was up to 102° on September 8; after that it was usually around 99° or 100°, with occasional rises to 100.5°. The patient died of uremia. At the postmortem examination there was found a bacteria-free lesion of the aortic valve, slight in extent, and a more marked lesion of the mitral valve. The spleen weighed 450 grams (15 ounces); Malpighian bodies were prominent.

Summary. Occurrence of tender nodules in the bacteria-free period of the disease; anemia; nephritic condition.

CASE XXI.—Period of observation from October 3, 1912, to December 6, 1912. Three blood-cultures were made, with negative results. This was a case which was taken by a number of observers to be one of Banti's disease. The patient, who was aged sixteen years, suffered for four months before admission from epistaxis, weakness, dyspnea, palpitation, swelling of the feet, and increasing pallor. Examination of the heart revealed mitral insufficiency. The spleen was large, being felt four fingers' breadth below the free border. Petechiæ developed during the course of the disease. The color of the face was pale, with a café-au-lait tint. The urine was grossly hemorrhagic from time to time. The specific gravity ranged from 1012 to 1016, and once was 1026. The quantity was from 450 to 1950 c.c. It usually contained erythrocytes and leukocytes, and albumin in fair quantity. Blood examination showed erythrocytes, 2,550,000; hemoglobin, 26 per cent., later 20 per cent.; leukocytes, 6200; polymorphonuclears, 62 per cent.; and later there were, leukocytes 5200, and polymorphonuclears 56 per cent. The temperature at first rose to 103°, later it was only 101°. The patient developed edema of the lower eyelids, vomited repeatedly, and died in a profoundly uremic condition. At the postmortem examination there were found lesions of the mitral valve and chordæ tendineæ. The spleen weighed 510 grams (17 ounces); the Malpighian bodies were prominent. The cultures made postmortem from the spleen and blood showed an organism corresponding to the coccus generally found in these cases of endocarditis. Spreads made from the lesions in the heart showed absolutely no organisms. It is probable that in this case we are dealing with a case in which the lesions had become bacteria-free or nearly so only a short time before the patient came under observation. The cocci found in the spleen and blood at the time of the postmortem examination may have been thrown out from a few cocci left in some part of the vegetations and from some organ in the body where they had remained in latent condition and had then multiplied after or shortly before death. The fact that no cocci could be found in the vegetations is quite definite proof that the patient was becoming free from the bacterial infection because, as a rule, in all cases in which cocci are found in the blood during life or in postmortem examination the vegetations are full of cocci.

Summary. Marked splenic enlargement; marked renal phenomena; severe anemia; some pigmentation of the face developing under observation.

CASE XXII.—Period of observation from December 3, 1912, to December 11, 1912. Only one blood-culture was taken in this case, and in that a typical pneumococcus was found. The case, nevertheless, belongs in the group of cases which are undergoing spontaneous healing, for reasons which will be given when the postmortem findings are discussed. This patient, who was aged fifteen years, stated that she had had, for five years, frequent attacks of cardiac palpitation and dyspnea. The feet were swollen on frequent occasions. Three weeks before admission she was suddenly seized with cardiac palpitation and weakness, and took to bed. She suffered from cough and expectoration, and these symptoms continued until the time of admission to the hospital. For the last eight or nine days before admission she had been jaundiced. Examination of the heart revealed the presence of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable and petechiæ were present. The quantities of urine were 500 to 600 c.c.; specific gravity, 1020 to 1022; hyaline and granular casts, and erythrocytes were present; bile was easily demonstrable. Blood-examination showed hemoglobin 48 per cent. The temperature remained around 100° until December 5, when it rose to 105°; on the following days it was up to 103°. This rise of temperature was due to a lobar pneumonia, of which the patient died. At the postmortem examination there was found a bacteria-free lesion of the auricle and mitral valve. The spleen was twice the normal size, and there were old infarctions present. The kidneys showed typical embolic glomerular lesions, all in the healed state. Because the lesions in the heart were rather old and bacteria-free, and because the embolic lesions in the kidney were all completely healed, and there was practically no temperature up to the time that the pneumonia developed, the writer is of the opinion that the presence of pneumococci in the blood was due to a lobar pneumonia developing in a person who was in the bacteria-free stage of subacute bacterial endocarditis.

Summary. Marked anemia; renal phenomena; terminal pneumonia.

THE NOGUCHI LUETIN REACTION IN SYPHILIS.[1]

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PERHAPS there is no disease which is characterized by a greater diversity of pathological lesions or is more protean in its manifestations than syphilis. With a clear history of infection and the existence of tell-tale lesions a definite diagnosis may be made without hesitation. A clear history, however, often cannot be elicited, nor are unmistakable lesions always present. The vague symptoms and signs which indicate the insidious development of internal lesions or the early stages of parasyphilitic conditions may suggest syphilis to the trained syphilographer, but in only too many instances a definite diagnosis is attended with insurmountable difficulties for the average practitioner.

In recent years the laboratory has come to the aid of the clinician in diagnosticating these obscure cases. The Wassermann test is a valuable addition to our armamentarium, but one that is infallible by no means. Certain cases of frank syphilis may never give a positive reaction; the sera of those suffering with leprosy, malaria, yaws, etc., may react positively; treatment may render negative the test despite the persistence of active manifestations; and, finally, in view of the technical knowledge required to properly perform the test, the results are not reliable unless the tests have been made by a trained serologist.

The examination of fresh preparations from active lesions may reveal spirochetes that are diagnostic, but this method is applicable only to lesions which by their objective characteristics alone should suggest syphilis to one who knows the disease. Furthermore, various mouth spirochetes may be confused with the specific treponema of syphilis unless the microscopist be an expert.

As neither clinical nor present laboratory methods are devoid

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